REMARKS

The present application is directed to devices and compositions for detecting and diagnosing infectious diseases. In particular, the application relates to the use of a transdermal delivery device to diagnose infectious diseases such as mycobacterial infections. In an effort to facilitate prosecution Claims 21-33 have been cancelled, and Claims 34-57 have been added. Support for the new claims can be found generally throughout the specification. No new matter has been added. Accordingly, following entry of the present amendment Claims 34-57 will be pending.

Rejection of Claims 21-23, 25-27 and 29 under 35 USC §102(a)

In the September 3, 2003 Office Action the Examiner rejected Claims 21-23, 25-27 and 29 under 35 U.S.C. §102(a) as being unpatentable over Katsuhide *et al.* (JP 09206092, electronic translation version). The Examiner stated that Katsuhide *et al.* disclose a transdermal delivery device comprising an antigen composition including a phosphate buffered solution for promoting transdermal delivery of the antigen, and a holding portion, i.e. plaster, which contains the antigen composition for use in delayed-hypersensitivity reaction measurement of immunity against infectious disease such as tuberculosis by a tubercle bacillus. The Office Action stated that the mycobacterial antigens disclosed in Katsuhide *et al.* include MPB64, MPB59, MPB70 and MPB80. In addition, the Office Action stated that Katsuhide *et al.* teach incorporating the composition with hydrophilic ointments such as glycerol or polyethylene glycol, infiltrated into a strap or plaster for contact and application onto skin of human or animal, a patch test, *i.e.*, to effect transdermal delivery of the antigen. After topical application of the ointment into the skin by a patch, an allergic reaction in the form of a hardening phenomenon on the skin is caused by the existence of the antibody to the said mycobacterial antigens. Applicants respectfully traverse.

In an effort to facilitate prosecution, Applicant has amended the relevant claims. Specifically, the amended claims now recite a transdermal delivery device consisting of a antigen in combination with a physiologically effective solution, wherein the physiologically effective solution is a polyoxyethylene sorbitan derivative. Katsuhide et al. fail to describe or suggest transdermal delivery device that consists of polyoxyethylene sorbitan derivative. As a result of

this amendment, the rejection of the claims under 35 U.S.C. §102(a) is rendered moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claim 24 under 35 USC §103(a)

In the September 3, 2003 Office Action, the Examiner stated that Claim 24 is rejected under 35 U.S.C. §103(a) as being unpatentable over Katsuhide *et al.* (JP 09206092, electronic translation version) in view of (1) Haga *et al.* (Tubercle and Lung Disease, June 1994, Supp. No. 1 (196), hereinafter "Haga-I" or (2) Haga *et al.* (Jpn. J. Med. Sci., Biol, 1996), hereinafter "Haga-II" .

As discussed above, Katsuhide *et al.* fail to disclose the use of polyoxyethylene sorbitan derivative as a critical component in the transdermal delivery device discussed therein. Neither Haga-I nor Haga-II both of which discuss various aspects of MPB64 remedy this deficiency and as a result the combination of these references does not obviate the invention as currently claimed. Applicant therefore respectfully requests reconsideration and withdrawal of these rejections under 35 U.S.C.§103(a).

Rejection of Claims 28 and 30 under 35 USC §103(a)

Claims 28 and 30 under 35 USC §103(a) as being unpatentable over Katsuhide *et al.* in view of Barchfield *et al.* (U.S. 5,709,879). The Examiner stated that Katsuhide *et al.* fail to teach polyoxyethylene sorbitan derivative as surfactant for use in the instant invention but that Barchfieild *et al.* disclose a combination of adjuvant components, *i.e.*, liposome/antigen components and emulsion components which act together to produce elevated immune responses. The Examiner stated that one of ordinary skill in the art at the time of the invention would have a reasonable expectation of success in incorporating the teaching of Barchfield *et al.* in combining specific surfactants into the transdermal device of Katsuhide *et al.* because Barchfield *et al.* specifically teach that TWEEN® surfactants are commercially known agents for use in adjuvant combinations. Applicant respectfully traverses for the following reasons.

Applicant maintains that Barchfield *et al.* specifically teach adjuvant formulations comprising two components: an antigen/liposome component and an oil-in-water emulsion. The liposomes are used in embodiments known as fusogenic liposomes wherein they fuse to a biological membrane. Furthermore, Barchfield *et al.* specifically teach a liposome or emulsion composition which is administered systemically and not administered transdermally (see for example column 27, lines 35-54). Applicant maintains that one skilled in the art would not have combined Barchfield *et al.* with the composition and methodology of Katsuhide *et al.* Applicant asserts that the combination of these references does not teach or suggest the transdermal diagnostic device of the present invention. Applicant therefore respectfully requests withdrawal of this rejection.

As is well known to those skilled in the art, the skin has increasingly become more recognized as an excellent portal for the delivery of pharmaceutical agents. One of the functions of the skin is to serve as a protective barrier and prevent the body from being damaged by outside agents. One might consider the skin as a giant sponge that captures unwanted chemicals and prevents their damage from occurring. In order for pharmaceutical agents to be delivered through the skin, reversible methods for altering the skin's barrier ability must be employed. Physical and chemical methods are employed to accomplish this task. Without altering the skin's barrier ability, only a few useful pharmaceutical agents can successfully penetrate the skin well enough to be beneficial.

Some of the reasons for preferring transdermal delivery of a pharmaceutical substance as opposed to other methods of delivery include the following: (1) necessity for delivering a high concentration of a pharmaceutical substance to a particular 'effected' area, (2) necessity for avoiding irritation to the gastrointestinal tract thereby avoiding complications such as bleeding, (3) necessity for bypassing the liver and its metabolism, allowing more of the active ingredient to be locally utilized and (4) necessity for localizing the effects of the pharmaceutical substance. Effective transdermal delivery also requires choosing a physiologically effective pharmaceutical carrier, i.e. penetration enhancer, or combination of carriers/enhancers for relevant pharmaceutical substances. In arriving at the appropriate composition, numerous parameters must be considered such as proportions, size of molecule/drug/agent being delivered, chemical interaction of molecule/drug/agent and carrier/enhancer, tolerance by recipient, non-

corrosiveness to the skin, rate of absorption, and rate of elimination of active ingredients from bloodstream. Given the complexity of all the limitations and considerations that must be taken into account, one skilled in the art would readily concede that the formulation of an effective transdermal delivery device for a pharmaceutical agent would not be one that was a matter of routine or simple deduction based on the composition of another pharmaceutical composition comprising similar components. It is readily apparent that the design and development of a transdermal diagnostic device for detecting infection, would entail the consideration of vastly different limitations and factors in comparison to the design and development of an vaccine that was to be delivered subcutaneously or intradermally.

As discussed above and in previous responses, Barchfield recites claims directed to vaccine compositions comprising (1) an antigenic substance in association with liposomes and (2) an oil-in-water emulsion; and methods for using the same. The oil-in-water emulsion comprises a muramyl peptide, a metabolizable oil, and optionally an additional emulsifying agent. Barchfield only mentions that TWEEN surfactants may be combined with a related sorbitan monoester or triester surfactants to promote emulsion stability. Accordingly what Barchfield teaches is distinctly different from the ointment system disclosed by Katsuhide and as a result, one skilled in the art would not combine the two. Furthermore Barchfield is irrelevant to the present invention since for the reasons previously discussed and also because the present invention does not involve any oil components or oil base components.

Applicants respectfully submit that Claims 28 and 30 cannot be rendered unpatentable over Katsuhide et al. in view of Barchfield under 35 U.S.C. 103(a). Katsuhide et al. fail to teach the use of polyoxyethylene sorbitan derivatives and although Barchfield happens to mention polyoxyethylene sorbitan monooleate, it does so in reference to a pharmaceutical composition that is so remote from the diagnostic patch of the present invention, that one skilled in the art would have no motivation (or success) in combining the teachings of the cited references to arrive at the present invention as currently claimed.

Conclusion

In conclusion, Applicant believes that the claims are in condition for allowance. A Notice of Allowance is therefore respectfully solicited. If the Examiner believes any

informalities remain in the application, which may be corrected by Examiner's Amendment, whether any other issues can be resolved by telephone interview, telephone call with the undersigned attorney at (404) 745-2463 is courteously solicited.

Respectfully submitted,

Sima Singadia Kulkarni

Sima Singadia Kulkarni
Registration No. 43,732

KILPATRICK STOCKTON LLP
Suite 2800
1100 Peachtree Street
Atlanta, GA 30309-2463
Telephone: (404) 745-2463
Our File: 19626-0112 (43925-259755)